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ALSTON & BIRD LLP
BANK OF AMERICA PLAZA
101 SOUTH TRYON STREET, SUITE 4000
CHARLOTTE, NC 28280-4000

| EXAMINER | |
|---|---|
| LI, BAO Q | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1648 | |

DATE MAILED: 04/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/019,644 | KAPPES ET AL. | |
| | Examiner | Art Unit | |
| | Bao Qun Li | 1648 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *06 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-5,7-10,12-16 and 51-60* is/are pending in the application.

4a) Of the above claim(s) *51-59* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-10,12-16 and 60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/28/2001*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

Claims 1-5, 9-10, 12-16 and 51-60 are pending.

### *Election/Restrictions*

1. In response to the previous Office Action on ***Election/Restrictions***, Applicants canceled claims 6-8, 11, 17-50 and added claim 60 that depends on claim 1. Applicants elect with traverse of group I, claims 1-5, 9-10 and 12-16 in Paper No. 11 is acknowledged. The traversal is on the ground(s) that group newly added claim 60 falls within the elected claim 1, as such, the examiner is respectfully requested to reconsider to rejoin the elected group I.

2. Applicants' argument has been respectfully considered, claim 60 is rejoined with the elected group I.

3. The rest of restriction requirement is still deemed proper and then made Final.

4. Claims 1-5, 9-10, 12-16 and 60 are considered before the examiner. Claims 51-59 are withdrawn from the consideration.

### *Claim Rejections - 35 USC § 112*

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-5, 9-10, 12-16 and 60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claim 1 is vague and indefinite for the following undefined and confused recitation: 1). What is the structure of a trans-viral vector system? 2). What may the viral particle comprise? and 3). What are the metes and bounds of one or more help function?

8. The claim is interpreted in light of the specification; however, the specification does not teach what the above recitations mean. Therefore, the claim is considered indefinite. This affects the decedent claims 3-5, 9-10, 12-16 and 60.

9. Claim 5 is vague and indefinite in that the metes and bonds of "one or more genetic element" are not defined. The claim is interpreted in light of the specification; however, the

specification does not give what the definitions of "other genetic element" are. Therefore, the claims are considered indefinite.

10. Claim 9 is also vague for recitation of a relative word "capable of", because the capability of a compound or composition to perform some function is merely a statement of a latent characteristic of said compound or composition and said language carries no patentable weight.

11. Moreover, claims 9 and 10 are still vague and indefinite in that the metes and bounds of " a nucleic acid sequence" are not defined. The claim is interpreted in light of the specification; however, the specification does not teach what the definitions of " a nucleic acid sequence" or " a retroviral nucleic acid sequence" are. Therefore, the claims are regarded as indefinite.

12. Claim 4 is vague and indefinite in that the metes and bounds of mobilization are not defined. The claim is interpreted in light of the specification; however, the specification does not give the definition of mobilization. The claim is considered indefinite.

***Claim Rejections - 35 USC § 102***

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 1, 3, 4, 9, 10, 12-13, 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Miller et al. (J. Virol. 1991, Vol. 65, No. 5, pp. 2220-2224).

15. Miller et al. disclose a method for generating a recombinant retroviral vector particle comprising to co-transfect a population of host cells with three DNA constructs. The first construct is plasmid pLGPS comprising a Moloney murine leukemia virus gag-pol genes under the control of the retrovirus promoter LTR, the second plasmid is pMOV-GalV encoding the envelope protein of gibbon ape leukemian virus; and a third plasmid is a pLN vector containing an antibiotics gene of neomycine and packaging signal that are regulated under the retroviral MoMLV LTR (See Fig. 1 on page 2221). In this content, the helper function of envelope protein is provided by trans with the second plasmid, and other helper function in provided by trans with other plasmid comprising a mutant methotraxate-resistant dihydrofolate reductase gene (dhfr) or

a hygromycine phosphotransferase (hpt) gene (See pages 2221), which helps to select the positive recombinant of above described retroviral genes. The antibiotics resistant gene is inherently integrated into the host cell genome. The step for detecting the positive retroviral recombinant genes is to examine the reverse transcriptase encoded by the pol gene (Se table 1 on page 2221). The gag gene in the fist construct besides the pol gene is considered as a cis-acting a retroviral coding sequences that facilitates reverse transcription and integration. The marker gene of Neo is controlled by a constitutive SV40 promoter or the inducible retroviral promoter LTR. While the intended use of the method disclosed by Miller et al. is not for detecting the retroviral recombinant, the method told by Miller is for generating the retroviral recombinant, it simply comprising the same steps as the current claims. As the limitation of the claimed intended use does not change the manipulation of the claimed method, the claimed invention, is inherently anticipated by the cited reference.

16. Claims 1, 3, 4, 9, 10, 12-13, 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Naldini et al. (Science 1996, Vol. 272, No. 5259, pp. 263-267).

17. Naldini et al. teach a method for generating a recombinant HIV vector particle comprising use of three plasmids to co-transfect a population of host cells. Plasmid pCMVΔR9 is a packaging construct comprising the human cytomegalovirus (hCMV) immediate early promoter that drives the expression of HCV gag and pol. The construct also comprises packaging signal ψ and other adjacent sequences that facilitate the expression of gag and pol as viral like particle, wherein the pol gene encodes the protease, reverse transcriptase and intergratase. The second plasmid encodes a heterologous envelope protein from either Moloney leukemia virus (MLV) or vesicular stomatitis virus (VSV G) that assist the formation of the pseudotyped retroviral particle. The third plasmid is a transducing vector (pHR) that contains cis-acting elements that are requires for packaging reverse transcripatase, integration, as well as unique restriction sites for the cloning of heterologous complementary DNAs (cDNAs). The last plasmid comprises nearly 350 base pairs of gag as well as env sequences encompassing the Rev responsive element (RRE) flanked by splice signals. The Escherichia coli β-gal or the firefly luciferase coding sequences were also inserted into pHR downstream of the hCMV promoter to serve as a reporter gene that indicates the positive recombinant by PCR or confocal microscope

technique. The confocal microscope in inherently uses FISH to stain the positive clone and detect the positive clone under the microscope (See entire document, especially page 263 and Figs. 2-4 on pages 265-266). While the intended use of the method disclosed by Miller et al. is not for detecting the retroviral recombinant, the method told by Miller is for generating the retroviral recombinant, it simply comprising the same steps as the current claims. As the limitation of the claimed intended use does not change the manipulation of the claimed method, the claimed invention, is inherently anticipated by the cited reference.

***Claim Rejections - 35 USC § 102***

18. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

19. Claims 1-5, 9-10, 12-13, 15-16 and 60 are rejected under 35 U.S.C. 102(a) as being anticipated by Kafri et al. (J. Virol. 1999, Vol. 73, No. 1, pp. 576-584).

20. Kafri et al. disclose a unique lentivirus packaging cell line and a method for generating a retroviral recombinant vector particle by using the cell line. The whole procedure for generating the lentivirus recombinant vector particle comprising to use three plasmids to transform the packaging cell line. The positive clone generated by the cell line is detected with a blue fluorescent marker gene expression, and the p24 antigen encoded by HIV gag gene expression (See Fig. 1 on page 578, Table 1 on page 579, and Figs. 3 and 4 on page 580-581). The three plasmids include the first plasmid is pPTK encoding a tetracycline-regulated transactivator (TA) regulated by CMV promoter, The second plasmid is inducible plasmid pBIGFG comprising VSV G envelope protein and green fluorescent protein (GFP) under the control of a bidirectional tetracycline-inducible promoter. Another plasmid is a vector comprising all HIV genes excluding the envelope gene. The first plasmid is used for transducing the host cell line to stably express the tetracycline-regulated transactivator (TA). The second plasmid is used for co-transfect with the first vector in host cells to make a pseudotyped retroviral vector. The helper function of the

marker gene and antibiotics envelope protein are all provided by trans from another plasmids. The other cis acting element of HIV contained within the same plasmid of HIV gag and pol, such as tat, Rev, nef Vpu, Vpu and Vif all assist the reverse transcriptase expression encoded by Pol gene (See entire documents, especially pages 576-577). While the intended use of the method disclosed by Kafri et al. is not for detecting the risk of forming RCR, it actually is a method for detecting the positive retroviral recombinant vector produced by the method, and it simply comprising the same steps as the current claims. As the limitation of the claimed intended use does not change the manipulation of the claimed method procedures, the claimed invention, is inherently anticipated by the cited reference.

***Claim Rejections - 35 USC § 103***

21. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

22. Claims 1-5, 9-10, 12-16 and 60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kafri et al. (J. Virol. 1999, Vol. 73, No. 1, pp. 576-584) as applied to claims 1-5, 9-10, 12-13, 15-16 and 60 above, and further in view of Morgenstern et al. (Nucleic Acids Research 1990, Vol. 18, No. 12, pp. 3587-3596) for claim 14.

23. Claimed invention is directed to a method for detecting a retroviral genetic recombinant encoding gag and pol polypeptides comprising a steps of introducing into the host cells a trans-viral vector comprising the gag and pol coding sequences and forming a viral particle by the help after transducer the host cells with other plasmids encoding the helper function, such as a envelope protein in trans. The other elements in cis in the gag/pol construct assist the reverse transcription and integration. The mobilization of the nucleic acid sequence of gag, or pol, or gag/pol recombinant or marker gene are measured by PCR, FISH, tat transfer, antigen-detection.

24. Kafri et al. disclose a unique lentivirus packaging cell line and a method for generating a retroviral recombinant vector particle by using the cell line. The whole procedure for generating the lentivirus recombinant vector particle comprises the use three plasmids to transfer the packaging cell line. The positive recombinant clone is detected with a blue fluorescent marker gene expression, and the p24 antigen encoded by HIV gag gene expression (See Fig. 1 on page 578, Table 1 on page 579, and Figs. 3 and 4 on page 580-581). The three plasmids include the first plasmid of pPTK encoding a tetracycline-regulated transactivator (TA) regulated by CMV promoter, a second plasmid of pBIGFG comprising VSV G envelope protein and green fluorescent protein (GFP) under the control of a bidirectional tetracycline-inducible promoter, and a third construct comprising all HIV genes excluding the envelope gene. The first plasmid is used for transducing the host cell line to stably express the tetracycline-regulated transactivator (TA). The second plasmid is used for co-transfecting with the third construct to make a pseudotyped recombinant retroviral particle. The marker gene and antibiotics gene provided by trans from another plasmids help to establish and select the positive recombinant clone. The other cis acting elements including tat, Rev, Nef, Vpu, Vpu and Vif all assist the reverse transcriptase expression encoded by Pol gene in the third construct (See entire documents, especially pages 576-577). Kafri et al. differ from the claimed invention in that they do not teach to use the puromycin as the drug resistant gene selection.

25. However, the use of puromycin drug resistant gene is a well-known method like use of other drug resistant gene, such as neomycine, in the art to select the positive recombinant clone. For example, Morgenstern et al. disclose a method for constructing retroviral vectors. They construct each of these retroviral vectors with one of four different dominantly acting drug selection markers including G418, hygromycin B, bleomycin/phleomycin and pyromycin, respectively (See abstract).

26. Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention was filled to be motivated by the recited reference of Kafri et al. and to combine the methods taught by Kafri et al. and Morgenstern et al. to make and select the positive recombinant retroviral vector by using pyromycin as a drug resistant gene with highly expected results. As there are no unexpected results have been provided, hence the claimed invention as a whole is prima facie obvious absence unexpected results.

***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 571-272-0904. The examiner can normally be reached on 7:00 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bao Qun Li
Art unit 1648
April 1, 2004

James C. Housel 4/2/04

JAMES HOUSEL
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600